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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,712	08/05/2002	Patrick Camilleri	P32329	1662

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,712	CAMILLERI ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-36,40 and 41* is/are rejected.

7)☒ Claim(s) *37-39* is/are objected to.

8)☒ Claim(s) *21-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/14/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application, filed 8/5/2002, is a 371 of PCT/GB00/02365 (WO 00/7654), filed 6/16/2000.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Objections

Claims 37-39 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites a method of transferring a DNA or RNA or "..analog thereof.." into cells. It cannot be determined how close to the DNA or RNA an analog might be, therefore the metes and bounds of the claimed subject matter are unclear. This rejection affects all dependent claims.

Claim 30 recites a method for "..genetic immunization..", then parenthetically "(for the generation of antibodies)..". These two methods differ in scope and it is unclear which method is claimed. The metes and bounds of the claimed subject matter are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-27, 31 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim methods to transfer DNA or RNA into eukaryotic and prokaryotic cells using a broad genus of compounds based on formula (I) in claim 21. Applicants disclose methods to transfect eukaryotic cells using compounds based on formula (II) in claim 36. The claims read on a genus of methods to transfect eukaryotic and prokaryotic cells using a broad genus of compounds.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. In the instant case, applicants only disclose the GS_G_1-9 compounds that appear to mediate transfection of CHO-K1 cells (Figs. 1 and 2). Neither applicants nor the prior art disclose transfection of prokaryotes by any molecules related to formula (I). Applicants claim the process of using compounds based on formula (I) for transfection of prokaryotes by function only, without a correlation between structure and function. The diversity of the compounds and methods claimed and lack of disclosure regarding whether or not they can transfect prokaryotic cells would require the skilled artisan to conclude that the examples presented by the applicants are not sufficient to describe the claimed genus.

Claims 21-27, 31 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transfection of eukaryotic cells using certain GS-G compounds, does not reasonably provide enablement for transfection of prokaryotic cells. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning transfection of prokaryotic cells with the claimed compounds is unpredictable. Transfer of nucleic acids into bacteria (transformation) is accomplished primarily by two methods: heat or cold shock in the presence of $CaCl_2$ (or other divalent cations); or electroporation (Sambrook et al, 1995). How either of these methods work is unknown, nor is the mechanism by which DNA enters competent *E. Coli* (pg. 1.74 of Sambrook, first paragraph). Hence, improvements on these protocols have occurred solely "..as a consequence of empirical experimentation" (also pg.1.74, first paragraph). Madigan et al (Biology of Microorganisms, 1997) disclose that many bacteria are naturally competent (able to take up external DNA) and therefore easily transformed with no manipulation (pg. 323, last paragraph). Other bacteria are transformed "..poorly or not at all under natural conditions" (pg. 324, first column) and how to induce such competence ".. may involve considerable empirical study". Neither applicants nor the prior art disclose transfection of prokaryotes by any molecules related to formula (I). Given the teachings of the art stated above and lack of disclosure of the

applicants regarding transformation of any prokaryote with the claimed compound(s), it is unpredictable that the compounds would function as claimed.

State of the art. The state of the art regarding the transfection of prokaryotic cells using compounds of formula (I) is poorly developed. The development of such compounds and methods would have to be done empirically.

Number of working examples. Applicants have provided a working example of two highly related compounds that differ only in *n* length (4 vs. 6 carbons), GS_G-6 and GS_G-1, that can be used in a method to efficiently transfect eukaryotic cells. Applicants have provided no working examples of compounds of formula (I) that can be used in methods to transfect prokaryotic cells.

Amount of guidance. Applicants provide no direction or guidance on how to transfect prokaryotic cells. The specification requires the skilled artisan to practice trial and error experimentation with a vast array of potential compounds and methods to determine which (if any) will be useful as claimed.

Scope of the invention. The claims are broad in nature and read on any and all transfection methods using compounds of formula (I).

Nature of the invention. The invention involves the unpredictable art of producing a transfection reagent for prokaryotic cells based on formula (I).

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Claims 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning antisense therapy, gene therapy, and DNA vaccination is unpredictable. Considering only a single application of antisense therapy (prostate cancer), Gleave et al (Ann. N.Y. Acad. Sci., 2003) list several drawbacks that currently exist, such as rapid degradation, complement activation, thrombocytopenia and immune stimulation to CpG motifs (page 98). They also state that a fraction of the 100,000 possible mRNA sequences found in the human genome (page 99) are possible targets for antisense therapy, yet applicants fail to identify a single one.

The art concerning expressing foreign DNA sequences in humans (gene therapy) is unpredictable and the field of gene therapy as a whole is also unpredictable, let alone the embodiments of the instant invention (Juengst, E.T., BMJ, 2003). Juengst states that clinical trials of gene therapy have not met with much success, have resulted in one iatrogenic death and "serious downstream disease" traceable to the gene therapy (p. 1410, second paragraph). Dang et al. (Clin. Cancer Res., Vol. 5, p. 471-474, 1999) outline several factors limiting human gene therapy such as suboptimal vectors, lack of long term and stable gene expression, and host immune response to the vector. They further cite the findings of the Orkin-Motulsky Committee, commissioned by the director of the NIH, that found human gene therapy an immature science with limited understanding of gene regulation and disease models. Applicants provide no disclosure regarding how to overcome these recognized problems, nor provide an example of a disease or gene suitable for the claimed method.

DNA vaccines have not been approved for use in humans and data from human clinical trials have not shown much promise (Berzofsky, J.A. et al., J. Clin. Invest. Vol. 113: p.1515-1525, 2004, in particular see page 1519, second column). As an example for a particular disease type, DNA vaccines have not demonstrated any convincing efficacy in the treatment of cancer (Restifo, N.P. et al., Gene Therapy, Vol 7: p.89-92, 2000).

State of the art. The state of the art regarding the use of compounds of formula (I) for antisense therapy, gene therapy, or vaccination is poorly developed. The development of such vectors, methods, and nucleotide sequences would have to be done empirically.

Number of working examples. Applicants have provided no working examples of methods using compounds of formula (I) in antisense therapy, gene therapy, or vaccination.

Amount of guidance. Applicants provide no direction or the claimed methods of antisense therapy, gene therapy, or vaccination. The specification requires the skilled artisan to practice trial and error experimentation with different vectors, diseases, and methods to determine which (if any) will be useful as claimed.

Scope of the invention. The claims are broad in nature and read on the therapy of any disease by introduction of any nucleotide sequence using any compound of formula (I).

Nature of the invention. The invention involves the unpredictable art of treating or curing any disease.

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-36 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Pestman et al (Langmuir, 1997, cited by applicants). The instant claims recite a compound that has the formula (I) (claim 32): wherein Y1 and Y2 may be the same or different and are carbohydrates; R1 and R2 may be the same or different and may be hydrogen, a C_{1-24} alkyl or alkyl carboxy group, or a carbon chain of 2-24 carbon atoms having one or more carbon/carbon double bonds; and *n* is from 1 to 10. R1 and R2 may be alkyl groups of C_{10-20} or C_{12-18} and *n* may be from 2 to 8 or from 4 to 6. The compound may be a gemini compound where R1 and R2 are the same and Y1 and Y2 are the same. The compound may also be formula (II) in claim 36. Also claimed is a process of making a compound of formula (I) comprising adding carbohydrate groups at the amine ends of an alkyl diamine compound.

Pestman et al disclose carbohydrate-based gemini surfactants that meet the criteria of formula (I) and formula (II) (see Fig. 1, pg. 6857). The structures disclosed in Fig. 1 have the open form of glucose at both Y positions, both R groups may be the same (hydrogen or a C_{14} alkyl group), and n may be from 6 to 10. The compounds are prepared by addition of carbohydrate groups (D-glucose) to diaminoalkane (page 6857, Experimental Section).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1636